REMARKS

As requested by the Examiner, a new Abstract commencing on a separate sheet, apart from any other text, has been presented.

Claim 23 has been amended to recite "[a] process for decoupling production of a target fermentation product from biomass production in a fermentation medium comprising: (a) providing a recombinantly produced microorganism from the genus Bacillus that has been engineered to contain a polynucleotide sequence which encodes biosynthetic enzymes for said target fermentation product, (b) introducing a mutation causing a biotin auxotrophy into the microorganism to control biomass production and which does not compromise the ability of the microorganism to produce said target fermentation product, and (c) supplying the medium with an unlimited amount of substrates required for the production of said target fermentation product and with a limited amount of biotin complementing the auxotrophy; wherein said target fermentation product is selected from the group consisting of riboflavin, pantothenic acid, thiamin, folic acid, and pyridoxine." Support for this amendment is found in original claim 23 and in the specification at, for example, page 7, line 17, page 8, lines 1-2, page 9, lines 13-17, and page 12, lines 14-22. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claim 24 has been amended to recite "[a] process according to claim 23 wherein step (b) comprises introducing a polynucleotide comprising a deletion-insertion mutation into the genome of the microorganism to disrupt the microorganism's ability to produce biotin." Support for this amendment is found in the specification at, for example, page 9, lines 12-17, page 12, lines 14-22, and in the Examples. (*Id.*).

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments respectfully is requested.

Declaration

The Examiner asserted that "[t]he oath or declaration is defective because non-initialed and/or non-dated alterations have been made to the address of inventor, Hans-Peter Hohmann." (Paper No. 20060313 at 2).

The undersigned contacted the Examiner on July 11, 2006 regarding the Examiner's objection to the declaration. The Examiner indicated that a revised declaration that is initialed and dated by inventor Hans-Peter Hohmann would be acceptable. With a view towards furthering prosecution, we enclose, as Exhibit 1, a revised declaration that is initialed and dated by inventor Hans-Peter Hohmann.

In view of the foregoing, the objection to the declaration is rendered moot. Accordingly, withdrawal of the objection is respectfully requested.

Abstract

The Examiner stated that "[t]he abstract of the disclosure filed October 8,2003 does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4)," and "[a] new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text." (*Id.*).

With a view towards furthering prosecution, as requested by the Examiner, a new Abstract commencing on a separate sheet, apart from any other text, has been presented. In view of the foregoing amendment, the apparent objection of the Abstract is rendered moot. Accordingly, withdrawal of the apparent objection is respectfully requested.

§112, First Paragraph Rejections

1. Enablement

Claims 23-32 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. (Paper No. 20060313 at 2). In making the rejection, the Examiner asserted that the specification "does not reasonably provide enablement for a process for decoupling production of a target fermentation product from biomass production in a fermentation medium comprising: (a) providing a recombinantly produced microorganism that contains a polynucleotide sequence which encodes biosynthetic enzymes for a target fermentation product, and (b) introducing an auxotrophy into the microorganism to control biomass production by limiting the concentration of a substrate complementing the auxotrophy in the fermentation medium; and a microorganism made by the process, where the structures of recombinantly produced microorganisms, target fermentation products and auxotrophy-causing polynucleotides are not identified." (*Id.* at 2-3).

The Examiner further asserted that the specification "only discloses cursory conclusions without data supporting the findings, which state that the present invention provides a process for decoupling production of a target fermentation product fiom biomass production in a fermentation medium." (*Id.* at 3).

The Examiner acknowledged, however, that the specification is enabling for "specific target fermentation" products and a specific auxotrophy, namely biotin:

> specification ... [is] enabling for a process for decoupling production of a specific target fermentation product (i.e., riboflavin) from biomass production in a fermentation medium comprising: (a) providing a recombinantly produced microorganism that contains a polynucleotide sequence which encodes biosynthetic enzymes for a target

> fermentation product (i.e., riboflavin), and (b) introducing a biotin auxotrophy into the microorganism to control biomass production by limiting the concentration of a substrate complementing the auxotrophy in the fermentation medium; and a microorganism made by the process, wherein the microorganism is a riboflavin production microorganism RB5O containing multiple copies of pRF69 and transformed with the polynucleotide sequence of SEQ ID NO: 1 .... (*Id.* at 2-3).

It is well settled that it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry her burden, the Examiner must identify and clearly articulate the factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370.

With a view towards furthering prosecution, we note that claim 23 has been amended to recite, *inter alia*, (1) that the recombinantly produced microorganism is a *Bacillus*, (2) that biotin is the specific auxotrophy, and (3) that riboflavin, pantothenic acid, thiamin, folic acid, and pyridoxine are the specific target fermentation products.

With these amendments, it is respectfully submitted that the Examiner's concerns regarding the scope of claims 23-32, *i.e.*, "unspecified variants regarding recombinantly produced microorganisms, target fermentation products and auxotrophy-causing polynucleotides," are rendered moot. (Paper No. 20060313 at 4).

Claim 23, as amended, is directed to a recombinantly produced *Bacillus* strain, which is exemplified in the specification by strain *B. subtilis* RB50. In view of the disclosure in the specification for the *B. subtilis* strain, a skilled person would certainly know how to manipulate other *Bacilli* strains in order to produce one of the claimed target fermentation products - riboflavin, pantothenic acid, thiamin, folic acid, or

pyridoxine - which all belong to the vitamin B complex and are thus also closely related to each others.

As acknowledged by the Examiner, the genes involved in the riboflavin biological pathway are well known in the art. (Paper No. 20060313 at 5, para. 3). Also the claimed target fermentation products are well known and available in the art. Thus, there would be no undue experimentation to take the information disclosed with regards to the *rib* genes over expressed as exemplified by *B. subtilis* RB50 and the guidance given in the specification regarding the introduction of biotin auxotrophy by mutating the microorganism, and arrive at applicants currently claimed invention. (*See, e.g.,* Specification at pages 12-18).

As is well accepted, even a "considerable amount" of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance. MPEP § 2164.05 and *In re Wands*, 8 USPQ at 1404. Here, as discussed above, the specification provides ample guidance, for the process recited in amended claim 23). (*See, e.g.,* Specification at pages 12-18). Accordingly, it is respectfully submitted that ample guidance is provided in the specification and for this reason alone, the rejection should be withdrawn.

It is also well established that claims must be separately analyzed. *Ex parte Jochim*, 11 USPQ2d 561 (BPAI 1988). Here, the Examiner has not referred to any specific features of any of the dependent claims that are insufficiently enabled. To the contrary, the Examiner has simply posited, in conclusory fashion, that, with respect to claim 23, "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

commensurate in scope with these claims." (Paper No. 20060313 at 3). Accordingly, it is respectfully submitted, for this additional reason, that the rejection should be withdrawn as to claims 24-32.

2. Written Description

Claims 23-32 have been rejected under 35 U.S.C. §112, first paragraph. (Paper No. 20060313 at 7). In making the rejection, the Examiner asserted that claims 23-32 "contain subject matter which was not described in specification ...." (*Id.* at 7). The Examiner further asserted that "the specification does not disclose a genus of variants for target fermentation products, recombinantly produced microorganisms that contain a polynucleotide sequence which encodes biosynthetic enzymes for a target fermentation product, and auxotrophy-causing polynucleotides. A single working example (culturing RB50::[pRF69]Bio' transformed with SEQ ID NO: 1 at different biotin concentration to produce riboflavin; Example 3) does not provide written description for the genus of variants in the claimed method." (*Id.* at 8).

The Examiner acknowledged, however, that the "the specification indicates that the invention provides a process for decoupling production of a target fermentation product from biomass production in a fermentation medium by introducing a specific biotin auxotroph mutant construct comprising SEQ ID NO: 1 into *bacillus subtilis* RB50 containing multiple copies of the engineered *rib* operon pRF69, culturing fermentations, and measuring biomass and riboflavin production at different biotin concentrations, which shows the product yield (i.e., the amount of riboflavin produced on the consumed glucose) is 33% higher in the decoupled process to the coupled process (see Examples 1-3) ...." (*Id.* at 7-8).

As is well accepted, there is a ***strong presumption*** that an adequate written description of the claimed invention is present in an application as filed. *See In re Werthheim*, 191 USPQ 90, 97 (CCPA 1976); and MPEP §2163(II)(A). Further, an applicant may show possession of the claimed invention by describing it using descriptive means such as, for example, words, structures, figures, diagrams and formulas. *See* MPEP §2163(I).

In addition, the written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species. *See Regents of University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); and MPEP § 2163 (II)(A)(3)(a)(ii). In fact, there are situations where ***even one*** species can adequately support a genus. *See Rasmussen,* 211 USPQ 323, 326-27 (CCPA 1981).

Initially, we note that claims 23-32 are original claims. Accordingly, as original claims, they are fully described, even in the absence of the extensive supporting disclosure in the specification. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973).

With a view towards furthering prosecution, however, claim 23 has been amended to recite, *inter alia*, (1) that the recombinantly produced microorganism is a *Bacillus*, (2) that biotin is the specific auxotrophy, and (3) that ribflavin, pantothenic acid, thiamin, folic acid, and pyridoxine are the specific target fermentation products.

With these amendments, it is respectfully submitted that the Examiner's concerns regarding the description in the specification for claims 23-32, *i.e.*, no alleged disclosure of "a genus of variants for target fermentation products, recombinantly

produced microorganisms that contain a polynucleotide sequence which encodes biosynthetic enzymes for a target fermentation product, and auxotrophy-causing polynucleotides," are rendered moot. (Paper No. 20060313 at 8).

In this regard, we note that the Examiner acknowledges the specification discloses "a process for decoupling production of a target fermentation product from biomass production in a fermentation medium by introducing a specific biotin auxotroph mutant construct comprising SEQ ID NO: 1 into *bacillus subtilis* RB50 containing multiple copies of the engineered *rib* operon pRF69, culturing fermentations, and measuring biomass and riboflavin production at different biotin concentrations, which shows the product yield (i.e., the amount of riboflavin produced on the consumed glucose) is 33% higher in the decoupled process to the coupled process (see Examples 1-3) ...." (Paper No. 20060313 at 7-8). The specification also discloses how to identify *Bacillus* strains that would fall within the scope of amended claim 23 (and, therefore, within the scope of dependent claims 24-32). The specification discloses, for example, at page 11, lines 17-20 the production rate of a microorganism carrying an auxotrophy; at page 12, lines 18-20 the specification discloses that a microorganism that is an auxotroph for biotin is unable to grow without supplementation with biotin (if the strain is a biotin-auxotroph); and at page 14, lines 8-11 the specification discloses an increase of 0.1% in the yield of the target fermentation product after engineering of the host microorganism. Therefore, there is sufficient information disclosed within the specification for one of skill to easily determine whether a strain would fall within the currently amended claims.

Moreover, a proper written description analysis requires an analysis of the understanding of an ordinarily skilled artisan at the time of the invention. *See* MPEP § 2163(II)(A)(2); *see also Wang Labs. v. Toshiba Corp.*, 26 USPQ2d 1767, 1774 (Fed. Cir. 1993). As noted above, the specification provides ample information detailing the knowledge in the art regarding the currently claimed process. (*See, e.g.,* Specification at pages 11-18 and Examples 1-3). In view of the foregoing, it is respectfully submitted that the Examiner has not properly taken into account this disclosure of information in determining whether the inventors were in possession of the currently claimed process at the time the application was filed. Thus, it is respectfully submitted that the Applicants were in possession of the full scope of the instantly claimed invention at the time the application was filed.

Accordingly, it is respectfully submitted that the rejection should be withdrawn.

Obviousness-type Double Patenting Rejection

Claim 32 has been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 6,656,721. (Paper No. 20060313 at 9-10).

The Examiner asserted that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because claim 32 in the instant application discloses a microorganism made by a process for decoupling production of a target fermentation product from biomass production in a fermentation medium comprising: (a) providing a recombinantly produced microorganism that contains a polynucleotide sequence which encodes biosynthetic enzymes for a target

fermentation product, and (b) introducing an auxotrophy into the microorganism to control biomass production by limiting the concentration of a substrate complementing the auxotrophy in the fermentation medium, wherein the step (b) can comprise introducing a polynucleotide sequence comprising SEQ ID NO: 1 into the microorganism; and the specification discloses the microorganism can be a riboflavin production microorganism RB50 containing multiple copies of the engineered *rib* operon pRF69 .... Thus, claim 32 in the present application and claim 9 in the patent are obvious variations of a riboflavin production microorganism RB50 containing multiple copies of pRF69, where the microorganism is transformed with the polynucleotide sequence of SEQ ID NO: 1." (*Id.*).

It is respectfully submitted that the rejection is incorrect as a matter of law and must be withdrawn. Claim 32, which is an original claim, was the subject of a restriction requirement in the parent application, U.S. Serial No. 09/633,927. (*See* Paper No. 5 at 2 (mailed October 31, 2001)). In particular, it was part of Group II, identified by the Examiner and subjected to restriction. Accordingly, the Examiner is prohibited by statute from making an obviousness-type double patenting rejection. *See* 35 U.S.C. § 121:

> A patent issuing on an application with respect to which a requirement for restriction under this section has been made, or on an application filed as a result of such a requirement, ***shall not*** be used as a reference either in the Patent and Trademark Office or in the courts against a divisional application or against the original application or any patent issued on either of them, if the divisional application is filed before the issuance of the patent on the other application. [Emphasis added).

Accordingly, withdrawal of this rejection is respectfully requested.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of all rejections and objections, and allowance of all claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 17, 2006.

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Respectfully submitted,

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